

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53539

Title: Primary sclerosing cholangitis with increased IgG4 levels: a distinct clinical subtype and its implications

Reviewer's code: 00051373

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-23

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-08 13:16

Reviewer performed review: 2020-03-09 13:09

Review time: 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

An interesting and clearly review to summarize the clinical phenotype, disease associations, differential diagnosis, response to therapy and pathogenic mechanisms underlying PSC-high IgG4 subtype.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53539

Title: Primary sclerosing cholangitis with increased IgG4 levels: a distinct clinical subtype and its implications

Reviewer's code: 00503623

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-23

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-09 14:06

Reviewer performed review: 2020-03-09 17:57

Review time: 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

This manuscript, 53539, provides the review of factors underlying primary sclerosing cholangitis (PSC), chronic progressive liver disease characterized by the elevated IgG4 subtype. Based on the extensive review of the available literature data, the conclusion is that PSC-high IgG4 has a distinct clinical phenotype from that of IgG-4-related sclerosing cholangitis (IgG4-SC), and hence requires careful assessment of clinical features, organ involvement and tissue morphology. This is an interesting contribution, which clearly lays out the methods for differential diagnosis of PSC from that of IgG4-SC. The paper is well written, and the presented data are amply justified by the accompanied figures and tables.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53539

Title: Primary sclerosing cholangitis with increased IgG4 levels: a distinct clinical subtype and its implications

Reviewer's code: 00068723

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Doctor, Occupational Physician

Reviewer's Country/Territory: Japan

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-23

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-09 08:39

Reviewer performed review: 2020-03-10 05:20

Review time: 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The authors performed systemic review of primary sclerosing cholangitis and IgG4. The manuscript was informative and useful. Figure 1 shows MRCP of IgG4-SC type 2. Was this photo referred from the literatures? Or was it from the authors' institute? If the photo was provided by the authors, it would be helpful to add clinical features to evaluate it. Was ERCP performed to the patient of Figure 1?

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53539

Title: Primary sclerosing cholangitis with increased IgG4 levels: a distinct clinical subtype and its implications

Reviewer's code: 02444986

Position: Editorial Board

Academic degree: MD

Professional title: Academic Research, Doctor, Professor, Research Scientist

Reviewer's Country/Territory: Turkey

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-23

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-09 08:07

Reviewer performed review: 2020-03-11 11:39

Review time: 2 Days and 3 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

Authors reviewed the literature in order to summarize the differences between 2 entities, namely PSC with increased IgG4 and IgG4 related SC. My comments: • Authors should have emphasized that this is not a generally accepted and so establish discrimination but, is a proposal for clinically subclassifying PSC based on the literature findings. • The manuscript must be redacted by omitting the repetitions and overlapping sections. • The resolution of figure 1 is inadequate, and the pathologic findings should be marked on the figure. • The expression of figure3 on page should be figure2, since there is no figure3.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53539

Title: Primary sclerosing cholangitis with increased IgG4 levels: a distinct clinical subtype and its implications

Reviewer's code: 00058381

Position: Editorial Board

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Austria

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-23

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-13 16:35

Reviewer performed review: 2020-03-14 06:34

Review time: 13 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This manuscript provides an overview on primary sclerosing cholangitis with increased IgG4 levels. The Core Tip should be shortened (according to the Guidelines for Authors). Section "Cholangiocarcinoma (CCA)": Ca-19-9 -> CA19-9. Section "Pathogenic Mechanisms in PSC high IgG4": A "Figure 3" is mentioned but not provided (- did you mean "Figure 2"?). Table 3: "If they then meet criterion R, then they diagnosis becomes definite" - this footnote requires correction. Figure legend 1 should be improved (with more information on your patient). Some sentences are grammatically unclear (e.g., Abstract, Results: "Serum IgG4:IgG1 ratios and novel IgG4:IgG RNA ratio report excellent discrimination but requires external validation", "The immunological drivers underlying prominent IgG4 antibodies in PSC are incompletely defined, although a role for HLA class-II, T-helper2 and T-regulatory cytokines and chemokines have been demonstrated").

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53539

Title: Primary sclerosing cholangitis with increased IgG4 levels: a distinct clinical subtype and its implications

Reviewer's code: 02860895

Position: Editorial Board

Academic degree: DSc, MD

Professional title: Chief Doctor, Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-23

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-09 01:31

Reviewer performed review: 2020-03-17 23:45

Review time: 8 Days and 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a comprehensive review article dealing with PSC with high IgG4 levels. I'd like to appreciate authors' effort for accomplishing this perfect work. I recommend add words 'systematic review' in the title to emphasize its perfectness. Again, the literature search strategy may become more easy to understand with illustrating it in a decision tree figure.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53539

Title: Primary sclerosing cholangitis with increased IgG4 levels: a distinct clinical subtype and its implications

Reviewer's code: 00039368

Position: Editorial Board

Academic degree: DA, PhD

Professional title: Academic Research

Reviewer's Country/Territory: Estonia

Author's Country/Territory: United Kingdom

Manuscript submission date: 2019-12-23

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-03-09 10:21

Reviewer performed review: 2020-03-18 12:12

Review time: 9 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a very well written and designed review paper concerning the analysis of clinical phenotype, differential diagnosis, response to therapy and pathogenic mechanisms associated with Primary Sclerosing Cholangitis (PSC) with elevated serum and/or tissue IgG4 subclass. The authors give an extensive overview about the prevalence, diagnosis of PSC with high level of IgG4, differential diagnosis of sclerosing cholangitis with high IgG4 levels and cholangiocarcinoma. The authors give very good overview about the pathogenic mechanisms in PSC with high IgG4 level, about genetic associations, the role of IgG4 antibodies, the role of cytokines and chemokines in pathogenesis. The authors conclude that PSC patients with high IgG4 levels have a distinct clinical phenotype and need discrimination from IgG4 related sclerosing cholangitis. The presence of IgG4 may represent chronic activation to persistent antigenic exposure in genetically predisposed individuals. The authors have reviewed and analyzed a large amount of literature (114 references). It should be mentioned that two Figures and 4 excellent Tables give a good overview about this topic.